In the Specification:

Please amend the title found on page 1, line 1 with the following:

PARTIALLY DEGLYCOSYLATED GLUCOCEREBROSIDASE POLYPEPTIDE AND CRYSTALS THEREOF

~~GAUCHER DISEASE DRUGS AND METHODS OF IDENTIFYING SAME~~

Please amend the paragraph beginning on page 2, line 32 with the following:

The enzyme glucocerebrosidase (EC 3.2.1.45, acid beta-glucosidase, D-glucosyl-N-acylsphingosine glucohydrolase, glucosylceramidase) is a peripheral membrane protein which hydrolyzes the beta-glucosyl linkage of glucosylceramide in lysosomes, thereby generating beta-glucose and ceramide (Figure 1a). This enzymatic activity requires the coordinate action of saposin C and negatively-charged lipids for maximal activity [Beutler E. and Grabowski GA., in: "The Metabolic and Molecular Bases of Inherited Disease", Scriver CR. *et al.* (eds.), McGraw-Hill Inc., pp. 3635-3668 (2001); Grabowski GA. *et al.*, 1990. Critical Rev Biochem Mol Biol. 25:385-414]. Based on sequence similarity, glucocerebrosidase is classified as a member of glycoside hydrolase family 30 (see website of ARCHITECTURE ET FONCTION DES MACROMOLECULES BIOLOGIQUES, France)~~http://afmb.enrs-mrs.fr/CAZY/GH_30.html~~).

Please amend the paragraph beginning on page 3, line 23 with the following:

Whole-enzyme replacement therapy with Cerezyme®, a recombinant variant of human glucocerebrosidase (Grabowski GA. *et al.*, 1995. Ann Intern Med. 122:33-9) is the main treatment for Type 1 Gaucher disease. Such treatment, however, is not curative, nor does it satisfactorily alleviate the symptoms of the disease. Furthermore, such whole-enzyme replacement therapy has numerous significant disadvantages, including: (i) administration of a molecule having various suboptimal pharmacokinetic characteristics, including suboptimal tissue penetration as a result of its large size; and suboptimal plasma membrane permeability and *in-vivo* half-life due to its polypeptidic composition; (ii) incapacity to correct endogenous glucocerebrosidase enzyme activity, and thereby incapacity to therapeutically confer such activity with optimal spatial (cell type/subcellular location), temporal, and activity level regulation; (iii) for optimal therapeutic results, the need to administer

the enzyme via injection, a painful, inconvenient, and expensive process; and (iv) elicitation of harmful immune responses against the administered enzyme in a substantial proportion of treated subjects as a result of its polypeptidic/modified oligosaccharide chemical composition (see entry for "Cerezyme" in the website of the Gaucher Registry ~~http://www.gaucherregistry.com/safety/cerezyme_pi.html~~). Hence, there is a clearly felt need for novel/improved Gaucher disease drugs.

Please amend the paragraph beginning on page 56, line 10 with the following:

Examples of suitable chemical structure databases for identifying the compound of the present invention include ISIS (see the website of MDL Information Systems, San Leandro, ~~http://www.molinfo.com~~), MACCS-3D (Martin, Y. C., 1992. J. Med. Chem. 35, 2145-2154), The Cambridge Structural Database (CSD; see the website of the Cambridge Crystallographic Data Center ~~http://www.ccdc.cam.ac.uk/prods/csd/csd.html~~), Fine Chemical Database (reviewed in Rusinko A., 1993. Chem Des Auto. News 8, 44-47), and the NCBI's Molecular Modeling DataBase: MMDB; ~~http://www.ncbi.nlm.nih.gov/Structure/MMDB/mmdb.shtml~~.

Please amend the paragraph beginning on page 56, line 26 with the following:

Ample guidance for computationally identifying a compound having a desired effect on an enzyme via software employing such "scanner" and "builder" type algorithms is available in the literature of the art (for example, refer to: Halperin I. *et al.*, 2002. Proteins 47, 409-43; Gohlke H. and Klebe G., 2001. Curr Opin Struct Biol. 11, 231-5; Zeng J., 2000. Comb Chem High Throughput Screen. 3, 355-62; and RACHEL: Theory of drug design, see New Drug Design website~~http://www.newdrugdesign.com/Rachel_Theory.htm#Software~~), and described in further detail hereinbelow.

Please amend the paragraph beginning on page 59, line 11 with the following:

Software programs useful for displaying such 3D structural models, include RIBBONS (Carson, M., 1997. Methods in Enzymology 277, 25), O (Jones, TA. *et al.*, 1991. Acta Crystallogr. A47, 110), DINO (DINO: Visualizing Structural Biology (2001) see the DINO website~~http://www.dino3d.org~~); and QUANTA, INSIGHT,

SYBYL, MACROMODE, ICM, MOLMOL, RASMOL and GRASP (reviewed in Kraulis, J., 1991. Appl Crystallogr. 24, 946).

Please amend the paragraph beginning on page 60, line 33 with the following:

Once the compound of the present invention is computationally identified it may be ordered from a commercial chemical library such as, for example, one held by a large chemical company such as Merck, Glaxo Welcome, Bristol Meyers Squib, Monsanto/Searle, Eli Lilly, Novartis, Pharmacia UpJohn, and the like. The compound of the present invention may also be ordered via the World Wide Web (Internet) via companies such as Chemcyclopedia (see the "mediabrains" website~~http://www.mediabrains.com/client/chemcyclop /BG1/search.asp~~). Alternatively, the compound of the present invention may be synthesized *de novo* using standard chemical and/or biological synthesis techniques, as appropriate to the molecular type. Ample guidance for synthesis of molecules typically identified via the above-described rational drug design methodology is provided in the literature of the art. For biological synthesis of molecules, such as polypeptides and nucleic acids, refer, for example to: Sambrook *et al.*, infra; and associated references in the Examples section which follows. For guidance regarding chemical synthesis of molecules, refer, for example to the extensive guidelines provided by The American Chemical Society (http://www.chemistry.org/ portal/Chemistry). One of ordinary skill in the art, such as, for example, a chemist, will possess the required expertise for chemical synthesis of molecules such as the compound of the present invention.

Please amend the paragraph beginning on page 63, line 5 with the following:

As used herein, "percent homology" between a test amino acid sequence and a reference amino acid sequence (e.g. SEQ ID NO: 1 or 8) corresponds to the "Positives" output obtained for the test sequence when using the reference sequence as input to perform a standard/default search of the protein-protein BASIC LOCAL ALIGNMENT SEARCH TOOL (BLAST) [blastp] software of the National Center for Biotechnology Information (see NCBI website) ~~(NCBI; http://www.ncbi.nlm.nih.gov/BLAST/)~~.

Please amend the paragraph beginning on page 86, line 6 with the following:

In summary, the catalytic domain of glucocerebrosidase consists of a $(\beta/\alpha)_8$ (TIM) barrel found also in the GH-A glycosidase clan~~—http://afmb.cnrs-mrs.fr/CAZY/GH_30.html~~. The catalytic residue E235 is H-bonded to H311 and Y313, and E340 is H-bonded to R120. The catalytic residues, E340 and E235, are hydrogen-bonded to R120 and to Y313 and H311, respectively, with the distance between the two glutamates consistent with a catalytic mechanism of retention. N370 is located on helix 7, which is at the interface of the TIM-barrel and a separate immunoglobulin-like domain on which L444 is located, implying a key regulatory or structural role for this non-catalytic domain.

Please amend the paragraph beginning on page 97, line 12 with the following:

Analyses are performed to identify which of the four carbohydrate chains have been removed by the glucocerebrosidase molecules deglycosylated under the different PNGaseF treatments. This is simply and conveniently analyzed since PNGaseF removes the whole glycosylation moiety attached to an Asn residue by cleaving the bond between the residue and the first sugar in the carbohydrate chain (N-acetylglucosamine; see Figure 5). Tryptic digests of the partially and fully glycosylated glucocerebrosidase are prepared, and the identity of the cleaved carbohydrate moieties is determined by mass spectrometry. These analyses are performed in the Weizmann Institute Center for Biological Mass Spectrometry, a unit established with three state of the art mass spectrometers ~~(http://bip.weizmann.ac.il/units/ms/mass.html)~~.

Please amend the paragraph beginning on page 101, line 1 with the following:

CD-ROM Content

The following CD-ROM is attached herewith:

Information provided as: File name / byte size / date of creation / operating system / machine format

The material included in the CD ROM is hereby entirely incorporated into the specification by reference